



No. 09/989,620
Amdt. dated June 11, 2003
Reply to Office Action of March 26, 2003

MARKED-UP VERSION OF THE AMENDMENTS TO THE CLAIMS

1. (Amended) A pharmaceutical composition comprising effective amounts of pharmacologically active agents, wherein said pharmacologically active agents comprise:

(a) an anti-human Fas antibody having an apoptosis inducing activity , said anti-human Fas antibody being monoclonal antibody CH11, monoclonal antibody HFE7A or a humanized antibody of monoclonal antibody CH11 or monoclonal antibody HFE7A; and

(b) a compound having a folate antagonistic activity or a dihydrofolate reductase inhibiting activity , said compound being methotrexate,

the relative amounts of said pharmacologically active [ingredients] agents (a) and (b) being such that [they] said pharmacologically active ingredients (a) and (b) exhibit a synergistic apoptosis inducing activity.

14. (Amended) A method for the [prevention or] treatment of a disease [preventable or treatable by an agent having apoptosis inducing activity,] selected from the group consisting of rheumatoid arthritis, chronic thyroiditis, allergic encephalitis, myasthenia gravis, hyperthyroidism, extreme insulin resistance in diabetes, rheumatic fever, human hemolytic anemias, granulocytopenias, thrombocytopenias and systemic lupus erythematosus comprising administering to a [mammal] human in

need thereof effective amounts of the following active ingredients:

(a) an anti-human Fas antibody having an apoptosis inducing activity , said anti-human Fas antibody being monoclonal antibody CH11, monoclonal antibody HFE7A or a humanized antibody of monoclonal antibody CH11 or monoclonal antibody HFE7A; and

(b) a compound having a folate antagonistic activity or a dihydrofolate reductase inhibiting activity , said compound being methotrexate,

the relative amounts of the active ingredients (a) and (b) being administered [being] such that [they] said active ingredients (a) and (b) exhibit a synergistic apoptosis inducing activity.

17. (Amended) The method according to claim [15] 14, wherein said anti-human Fas antibody having apoptosis inducing activity is [a] the monoclonal antibody CH11 or a humanized antibody thereof.

18. (Amended) The method according to claim [15] 14, wherein said anti-human Fas antibody having apoptosis inducing activity is [an anti-human Fas] the monoclonal antibody HFE7A which is produced by a mouse-mouse hybridoma HFE7A (FERM BP-5828) or a humanized antibody thereof.

27. (Amended) The method according to claim [15] 14, wherein the anti-human Fas antibody is administered in a daily dosage of 0.001 to 10 mg/kg and the compound having a folate antagonistic activity or a dihydrofolate reductase inhibiting activity is administered in a daily dosage of 0.15 µg/kg to 0.15 mg/kg.

28. (Amended) A method for the [prevention or] treatment of a disease [preventable or treatable by an agent having apoptosis inducing activity,] selected from the group consisting of rheumatoid arthritis, chronic thyroiditis, allergic encephalitis, myasthenia gravis, hyperthyroidism, extreme insulin resistance in diabetes, rheumatic fever, human hemolytic anemias, granulocytopenias, thrombocytenias and systemic lupus erythematosus comprising administering to a [mammal] human in need thereof effective amounts of a medicament in the form of a solution comprising pharmacologically active agents together with a diluent therefor, wherein said pharmacologically active agents comprise:

(a) an anti-human Fas antibody having apoptosis inducing activity selected from the group consisting of [a] monoclonal antibody CH11, [and] monoclonal antibody HFE7A [, or] and a humanized antibody [thereof] of the monoclonal antibody CH11 or the monoclonal antibody HFE7A, in a concentration of 0.1 to 100 ng/ml; and

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(b) methotrexate at a concentration of 0.05 to 5 nM,
the relative amounts of said pharmacologically active
[ingredients] agents (a) and (b) being such that [they] said
pharmacologically active agents (a) and (b) exhibit a synergistic
apoptosis inducing activity.